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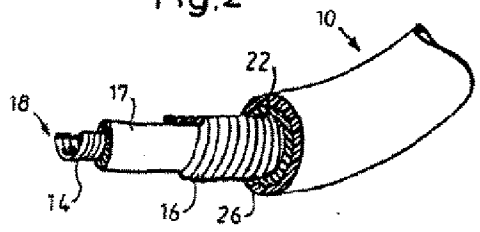
(54) Electrode cable

(57) The invention relates to an electrode cable (12) intended for implantation in a body cavity. The cable contains at least one elongate electrical conductor (14, 16) whose distal end section (10) has an essentially J-shape in the unrestricted state and a distal end electrode. The conductor (14) forms a channel (18) for the introduction of a stylet for governing cable stiffness and the configuration of the distal end section (10) during implantation. According to the invention, a biodegradable, biocompatible polymer material (26) is arranged on the exterior of at least the J-shaped distal end section (10) of the electrode cable.

Fig.2



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Description

TECHNICAL FIELD

The present invention relates to an electrode cable intended for implantation in a body cavity, especially for intracardiac stimulation and/or sensing heart signals, containing at least one elongate, flexible electrical conductor with a proximal end and, in the unrestricted state, and essentially J-shaped distal end section with an electrode for fixation to tissue in a heart wall, especially the upper atrial wall, and a channel for insertion of a stylet for governing the stiffness of the electrode cable and the configuration of the distal end section of the electrode cable during implantation.

THE PRIOR ART

Electrode cables intended for implantation in the right atrium of the heart normally have an essentially J-shaped distal end section to permit the anchoring of the end of the electrode in an upper part of the myocardial wall of the atrium. Here, the J configuration can be pre-shaped to assume a J shape in the unrestricted state, a stylet being introduced into a central channel of the electrode cable in implantation to straighten out the J bend and stiffen the electrode cable during the introductory phase of implantation. The stylet is thereupon withdrawn to permit the distal end section to rebound back into the J shape for fixation of the section in the upper part of the atrium. Examples of such electrode cables are shown and described in US-A-3 890 977 and US-A-4 496 561.

However, these J bends on the distal end of the electrode cable give the distal end section a residual stiffness, causing it to exert increased pressure on the heart wall, pressure which could irritate and damage the heart wall in some instances, thereby raising the threshold value, i.e. the voltage required to make the heart beat.

SUMMARY OF THE INVENTION

One object of the present invention is to eliminate the said shortcoming and propose an electrode cable which, despite a distal end section with a pre-formed J shape, offers a relatively soft and gentle J shape after implantation.

For this purpose, the aforementioned electrode cable according to the invention is characterized by a biodegradable, biocompatible polymer material, arranged on the exterior of at least the distal, J-shaped end section of the electrode, which before and during implantation is devised to strive to maintain an essentially J-shaped configuration for the distal end section but which dissolves after implantation, through contact with body fluid (blood), in order to create a soft, flexible, distal end section on the electrode cable.

The biodegradable material is appropriately in the form of a tubular sleeve which encloses at least the distal end section of the electrode cable.

Examples of biodegradable, biocompatible polymer materials, which could be used in an application according to the present invention, are stated in the dependent patent claims 4-6.

The invention will now be described in greater detail, referring to the attached drawing.

FIGURES

FIG. 1 is a schematic view of a pre-shaped, J-shaped distal end section of a bipolar electrode cable, and

FIG. 2 shows a partially opened perspective view of the circled section in FIG. 1.

PREFERRED EMBODIMENT

FIG. 1 shows a J-shaped end section 10 of a bipolar electrode cable 12 according to the invention. As shown in detail in FIG. 2, the electrode cable 12 is made of an inner, helically coiled conductor 14 and an outer conductor 16, coaxial to the inner conductor 14, the conductors 14, 16 being separated by an insulating, tubular sleeve 17. The inner conductor 14 forms a central channel 18, intended to admit a stylet (not shown) during implantation in order to stiffen the electrode cable during the latter's introduction through veins into the heart atrium and straighten out the J bend on the distal end section.

The outer conductor 16 is connected to a ring electrode 20 (anode) located at a distance from the tip of the J bend and is enclosed in an insulating sleeve 22 made of e.g. silicone rubber. The inner conductor 14 is connected to an end electrode 24 (cathode) located on the tip ahead of the ring electrode 20 and ahead of anchoring fins 25.

An additional tubular sleeve 26, devised to give the distal end section 10 of the electrode cable 12 an essentially J-shaped configuration in the unrestricted state, is arranged over the sleeve 22. This tubular sleeve 26 is made, according to the present invention, of a biodegradable, biocompatible polymer material, covering at least the distal end section 10, but it could also cover the entire length of the electrode cable 12 from a proximal end to the digital end. This means that the distal J-shaped end section 10 of the outer tubular sleeve 26, after being introduced in the essentially straight state, strives to resume its original J shape, when the stylet is removed from the channel 18 in implantation.

Instead of being devised as a tubular sleeve 26, the biodegradable polymer material can also be devised as bands or strips extending along the exterior of the shell 22, at least in the J-shaped distal end section 10 of the electrode cable, within the scope of the invention.

After a time, when the tip section of the electrode cable 12 has had time to become embedded in the atrial wall, the polymer material in the outer sleeve 26 will

have dissolved through contact with blood, thereby leaving behind a soft, flexible electrode cable which is gentle to the heart wall.

The degradation time for the sleeve 26 can range from one day up to one or more months.

The biodegradable polymer material can be selected from e.g. the groups proteins/amino acid polymers, poly(hydroxycarboxyl acids) and/or carbohydrate polymers. The proteins/amino acid polymers group can contain gelatin, collagen, polyserine, polythreonine, polyphenylalanine or the like. The poly(hydroxycarboxyl acids) group can contain polylactides and/or polyglycolides. The carbohydrate polymers group can contain dextran, starch, hyaluronic acid, cellulose or the like.

Claims

1. An electrode cable intended for implantation in a body cavity, especially for intracardiac stimulation and/or sensing of heart signals, containing at least one elongate, flexible electrical conductor (14, 16) with a proximal end and, in the unrestricted state, an essentially J-shaped distal end section (10) with an electrode (24, 20) for fixation to tissue in a heart wall, especially the upper part of the atrial wall, and a channel (18) for insertion of a stylet for governing cable stiffness and the configuration of the distal end section (10) of the electrode cable during the electrode cable's (12) implantation, **characterized** in that a biodegradable, biocompatible polymer material (26) which, before and during implantation, is arranged to strive to maintain a mainly J-shaped configuration for the distal end section (10) of the electrode cable (10) but which, after implantation, is dissolved by contact with body fluid to make the distal end section (10) soft and flexible, is arranged on the exterior of at least the J-shaped distal end section (10) of the electrode cable (12).

2. An electrode cable according to claim 1, **characterized** in that the biodegradable material is devised as a tubular sleeve (26) which encloses at least the distal end section (10) of the electrode cable (12).

3. An electrode cable according to claim 2, **characterized** in that the tubular sleeve (26) is made of a biodegradable material which covers the entire electrode cable (12) from its proximal end to its distal end.

4. An electrode cable according to any one of claims 1-3, **characterized** in that the polymer material is selected from the groups proteins/amino acid polymers, poly(hydroxycarboxyl acids) and/or carbohydrate polymers.

5. An electrode cable according to claim 4, **characterized** in that the proteins/amino acid polymers group contains gelatin, collagen, polyserine, polythreonine, polyphenylalanine or the like.

6. An electrode cable according to claim 4, **characterized** in that the poly(hydroxycarboxyl acids) group contains polylactides and/or polyglycolides.

7. An electrode cable according to claim 4, **characterized** in that carbohydrate polymers group contains dextran, starch, hyaluronic acid, cellulose or the like.

8. An electrode cable of any of claims 1-7, **characterized** in that the polymer material has a degradation time exceeding at least 24 hours.

Fig.1

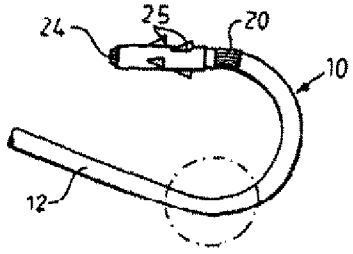
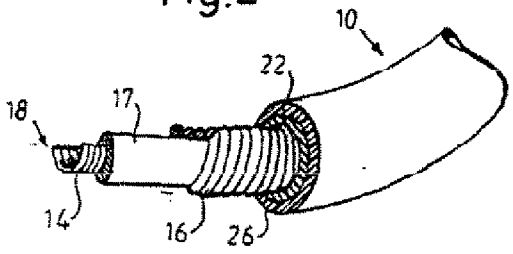


Fig.2



European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 96 85 0218.7

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.6)
A	US 4258724 A (ROGER BALAT ET AL), 31 March 1981 (31.03.81) * abstract * --	1-8	A61N 1/05
A	EP 85967 A1 (CORDIS CORPORATION), 17 August 1983 (17.08.83) * abstract * --	1-8	
A	EP 652017 A1 (A. STEMBERGER), 10 May 1995 (10.05.95) * abstract * -----	1-8	

TECHNICAL FIELDS SEARCHED (Int. Cl.6)

A61N

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
STOCKHOLM	22 April 1997	KARIN SÄFSTEN

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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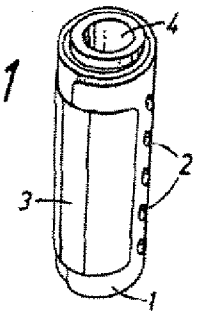
(54) Sustained drug release device for veterinary use.

(57) Device for oral administration of a medicament to a ruminant animal comprises a trilaminate sheet (1) containing the medicament rolled into a tube retained in the rolled configuration by a film (3) of material which disintegrates in the rumen to allow unrolling of the sheet. The tube ends are closed by plugs (2) which keep the tube closed during passage of the device through the oesophagus.

FIG.1



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VETERINARY DEVICES

This invention relates to devices for administration of veterinary preparations for ruminant animals.

Ruminant animals, particularly cattle and sheep, form an important group of animals which require periodic administration of veterinary medicines for the treatment and alleviation of various conditions. For example, it is often desirable to treat such animals, either therapeutically or prophylactically, with mineral or vitamin supplements, antibiotics, systemic insecticides, detergents for the relief of cattle bloat, and/or anthelmintics or other anti-parasitic agents. The repeated administration of such veterinary medicines to animals at frequent time intervals is expensive and inconvenient. There is therefore much need for a dosing system to be devised which would efficiently supply the veterinary medicine during prolonged periods of time after administration of a single preparation.

British Patent No.: 1318259 describes a number of devices for retaining slow release veterinary medicament formulations in the rumen over an extended period of time, thereby achieving the desired result. This prolonged retention in the rumen is obtained by the devices having a relatively narrow first configuration which allows the devices to be administered per os to the ruminant, and a relatively broad second configuration which the devices assume or are caused to assume in the rumen thereby hindering or preventing their passage out of the rumen. A typical example of such a device specifically described in said patent 1318259 is a plastic cylindrical capsule containing a detergent for the control of bloat in cattle. The capsule is 150 mm long and 30 mm wide (thereby allowing per os administration), and consisting of two half-cylinders hinged along one edge. The hinges are made from rubber and are biased so that the two half-cylinders spring apart in the rumen and thus become too wide to pass out through the rumen or to be regurgitated through the oesophagus. Each half-cylinder contains a gel of ethyl cellulose containing the desired anti-bloat agent which is leached from the gel by the rumen fluids over an extended period of time. The hinges are constructed so that under the rumen conditions they pull away from the half-cylinders after effective release of the agent thereby facilitating regurgitation of the fragmented device.

Other veterinary devices intended to achieve the same result are described in European Patent Applications Nos. 10987A and 21758A. These devices may comprise a flexible carrier sheet rolled into an open-ended tube-like configuration which is generally cylindrical, the sheet being constrained in that configuration by strips of gummed paper or similar means which are released when the preparation enters the rumen and becomes immersed in the rumen fluids. Typical dimensions of the cylinder formed by the sheet in its rolled-up condition are 3 cm diameter and 10 cm length. The preparation in its cylindrical state may be administered to the animal by means of a balling gun and enters the rumen through the oesophagus. In the rumen the constraining means become released and the sheet unrolls to an opened, relatively broad configuration in which it remains in the rumen and cannot escape. The sheet contains a medicament which is discharged into the rumen fluid over a period of time and the sheet is adapted to discharge the medicament at a predetermined rate. One such sheet is described in European Patent Application No. 0153070A and comprises a plastics core layer providing a matrix containing the medicament coated on its major surfaces with an inert plastics coating to form a trilaminate, the trilaminate having a pattern of perforations through which the medicament is discharged in the rumen. The rate of discharge of the medicament is determined primarily by the number and size of the perforations.

It has been found that such open-ended rolled-up sheet devices, while operating efficiently after entering the rumen, may become stuck in the oesophagus when administered to ruminants, particularly small calves, and are not ejected by the natural regurgitation action of the animal. The constraining means may then be released in the oesophagus and the sheet become unrolled so that it becomes impacted and cannot be removed. Permanent obstruction of the oesophagus in this way has serious consequences for the animal and is normally fatal.

Attempts have been made to avoid this problem by providing increased lubrication for the preparation, for example by coating it with corn oil or polyethylene glycol wax to ease its passage into the rumen. However, it has been found that impaction of the preparation in the oesophagus still occurs in a significant proportion of the animals treated.

The present invention is intended to provide a pharmaceutical device which avoids or alleviates this problem. According to one aspect of the invention, a device for oral administration of a medicament to a ruminant animal comprises a sheet of flexible material containing the medicament and capable of slow release of the medicament within the rumen, the sheet being rolled or folded into a tube configuration and constrained in that configuration by means releasable on contact with rumen fluids so that the sheet may unroll or unfold after

insertion in the rumen and remain therein, the ends of the tube formed by the sheet being provided with closing means allowing said unrolling or unfolding of the sheet in the rumen, said closing means keeping the tube ends closed during administration of the device and passage thereof into the rumen.

It has been found that when the ends of the tube are closed as the device passes through the oesophagus there is little or no risk of the device becoming impacted therein. The device in its rolled or folded condition normally passes through into the rumen, but if it fails to do so the device is regurgitated from the oesophagus spontaneously by the animal.

The tube ends should be closed by means which are retained by the device sufficiently firmly to prevent the closing means being released from the device before it enters the rumen, but which do not interfere with the unrolling or unfolding once the constraining means is released. The closing means may comprise of plugs extending into the ends of the tube and engaging its inner surface, preferably by a simple interference fit which is sufficiently tight to retain the plugs in place when the device is administered and passes through the oesophagus. The plugs may be made of any biologically acceptable material and may be of plastics material such as polyethylene.

In one embodiment, the closing means comprises such plugs having a cylindrical body portion provided with at least one radially projecting external rib, the rib diameter being such that it engages the tube inner surface to retain the plug in the tube. The rib may have an angled outer surface which diverges radially towards the tube end and terminates in a relatively sharp edge. The plug may then slide relatively easily into the tube but will require a significant pulling force to remove it from the tube. The plug may have a radially extending outer flange at its end to abut the edge of the sheet at the end of the tube.

The plug may be inserted into the tube end after rolling or folding of the sheet, alternatively the sheet may be rolled around a pair of suitably positioned end plugs which act as a spindle.

A device according to one embodiment of the invention will now be described by way of example with reference to the accompanying drawings in which:

Figure 1 shows the device in the rolled-up condition for administration to ruminant animals;

Figure 2 shows a trilaminate sheet to be rolled up to form the device of Figure 1;

Figure 3 shows an end plug for the device of Figure 1;

The sheet 1 shown in Figure 2 is a trilaminate sheet of the kind described in EP 0153070. It comprises a central resilient core sheet of ethylene vinyl acetate polymer (EVA) which is impregnated with morantel tartrate. This core sheet is coated on its upper and lower surfaces, but not its edges, with surface layers of pure EVA. The sheet is provided with a pattern of holes, two of which are punched through the trilaminate. Typical dimensions of the sheet are about 21 cm length, about 9.5 cm width and an overall thickness of 2.15 mm made up of the core having a thickness of 1.91 mm and the surface layers each of 0.12 mm thickness. The holes may be of 2.7 mm diameter.

The EVA of the core provides a matrix containing the morantel tartrate. The weight of morantel tartrate is approximately equal to the weight of EVA in the core and the device shown in the drawing contains about 11.6 g of morantel as the tartrate salt.

When the trilaminate sheet is present in the rumen of an animal the rumen fluids make contact with the core at the edges of the sheet and in the holes, but not over the main surface of the core which is protected by the EVA coating which acts as a barrier layer. The morantel tartrate is then slowly released into the rumen through the edges of the sheet and the holes, the rate of release depending on the number of holes. The rate of release of morantel tartrate into the rumen is substantially uniform and may be complete after a period of 90 days in the rumen. The trilaminate sheet remains substantially intact during release of the morantel tartrate and then gradually disintegrates within the rumen.

In order to allow administration to the animal the trilaminate sheet is rolled into a cylindrical configuration as shown in Figure 1 and is retained in this configuration by a sheet (3) of adhesive regenerated cellulose film which surrounds the cylinder sides completely and prevents the sheet unrolling until the sheet enters the rumen. The cylinder has an outer diameter of about 2.53 cm and may be administered to the animal in known manner by use of a balling gun. Once in the rumen, the cellulose film disintegrates and the trilaminate sheet unrolls under the effect of its resilience and remains in the rumen. Both ends of the cylinder are closed by circular hollow plugs (4), one of which is shown in Figure 3. The plugs are formed of a physiologically harmless plastics material such as polyethylene and comprise a pointed cylindrical body (5) having a flange (6) at its outer end and a pair of circumstantial ribs (7) and (8) having angled outer surfaces (9) and (10) which diverge radially outwardly towards the flanged outer end of the plug. The diameter of the plug body is such that it may fit tightly into the tube formed by the rolled-up sheet (1); in the embodiment shown the body (5) has an outer diameter of 9.89 mm and the maximum diameter of the ribs is 13.70 mm. The materi-

ais of the plug and the sheet both have a certain degree of resilience and the diverging shape of the ribs is such that the plug may readily be inserted in the tube formed by the sheet, the flange (6) abutting the end of the rolled tube, and after insertion the plug is retained in the tube by the ribs (7) and (8).

As the plugs are firmly retained in the tube, they remain in place when the device is administered to an animal and passes through the oesophagus to the rumen. As the device uncoils in the rumen the plugs are released and become detached from the sheet (1) so that they do not interfere with the action of the sheet in discharging morantel tartrate in the rumen. The plugs are eventually discharged from the rumen, together with the remains of the disintegrated sheet, by natural processes. It has been found that when the device is administered to calves, the incidence of impaction in the oesophagus is substantially zero.

Claims

1. A device for oral administration of a medicament to a ruminant animal comprising a sheet of flexible material containing the medicament and capable of slow release of the medicament within the rumen, the sheet being rolled or folded into a tube configuration and constrained in that configuration by means releasable on contact with rumen fluids so that the sheet may unroll or unfold after insertion in the rumen and remain therein, characterised in that the ends of the tube formed by the sheet are provided with closing means allowing said unrolling or unfolding of the sheet in the rumen, said closing means keeping the tube ends closed during adminstration of the device to the animal and passage thereof into the rumen.

2. A device according to claim 1, in which the closing means comprise plugs extending into the ends of the tube and engaging the inner surface thereof.

3. A device according to claim 2, in which the plugs engage said inner surface by an interference fit.

4. A device according to claim 3, in which the plugs have a cylindrical body portion provided with at least one radially projecting external rib, the rib diameter being such that the rib engages the tube inner surface to retain the plug in the tube.

5. A device according to claim 4, in which the rib has an angled outer surface which diverges radially towards the tube end and terminates in a relatively sharp edge.

6. A device according to any one of claims 2 to 5, in which the plug has a radially extending outer flange at its end to abut the edge of the sheet of the end of the tube.

7. A device according to any one of the preceding claims, in which the sheet comprises a perforated triaminate of plastics containing said medicament, the sheet being rolled into a cylinder configuration and retained in that configuration by a film of material capable of disintegrating within the rumen surrounding the cylinder sides.

8. A method of administering a medicament to a ruminant animal, which comprises inserting a device according to any one of the preceding claims in the rumen through the oesphagus.

9. A method of making a device for oral administration of a medicament to a ruminant animal which comprises rolling or folding into a tube configuration a sheet of flexible material containing the medicament capable of slow release of the medicament within the rumen, constraining the sheet in said configuration by means releasable on contact with rumen fluids so that the sheet may unroll or unfold after insertion in the rumen and remain therein, and providing the ends of the tube with closing means allowing unrolling or unfolding of the sheet in the rumen, the closing means keeping the tube ends closed during administration of the device to the animal and passage thereof into the rumen.

10. A method according to claim 9, in which the closing means comprise plugs extending into the ends of the tube and either the plugs are inserted in the tube ends after rolling or folding of the sheet, or the sheet is rolled around the plugs to form a tube.

FIG. 1

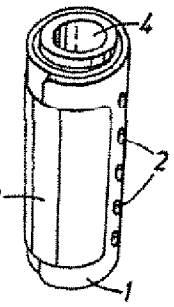

FIG. 2

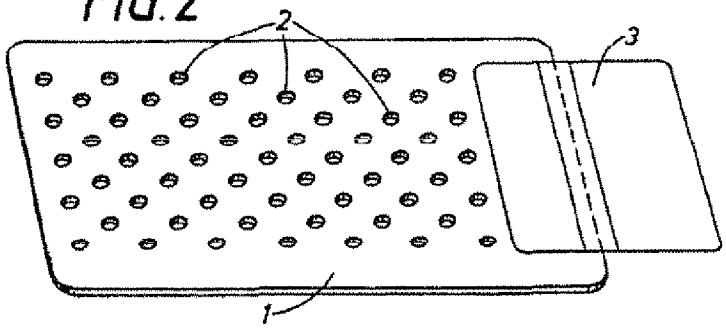

FIG. 3